**IN THE UNITED STATES DISTRICT COURT**
**FOR THE DISTRICT OF DELAWARE**

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| NOVARTIS PHARMACEUTICALS CORPORATION,<br>Plaintiff,<br>v.<br>ACCORD HEALTHCARE INC., et al.,<br>Defendants. | C.A. No. 1:18-1043-KAJ |

**HEC PHARM CO., LTD. AND HEC PHARM USA INC.'S MOTION FOR PARTIAL STAY OF THE FINAL JUDGMENT AS TO A RESET OF FINAL APPROVAL OF HEC'S ANDA UNDER § 271(E)(4)(A)**

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## INTRODUCTION

HEC received final FDA approval for its generic fingolimod in December 2019.[1] On September 11, 2020, following a trial on the merits, this Court entered Final Judgment, finding Novartis' U.S. patent No. 9,187,405 (the "'405 patent") valid and infringed, and permanently enjoining HEC from selling or importing generic fingolimod. Dkt. 780. HEC will appeal this Court's order to the Federal Circuit as to the '405 patent's validity, and the validity issues will likely be resolved before the end of 2021. However, under the judgment, "[p]ursuant to 35 U.S.C. § 271(e)(4)(A), the effective date of any final approval by the United States Food and Drug Administration of HEC's ANDA No. 207939 shall be a date not earlier than the expiration date of the '405 Patent . . ." [Dkt. 780 (¶3)] - and the '405 patent expires on June 25, 2027. Most distressing, the FDA may unilaterally revoke final approval of HEC's ANDA, thus sending HEC back to square one, requiring HEC to once again seek FDA final approval, regardless of any appellate decision as to validity. Such an outcome would irreparably injure HEC, possibly keeping it off of the market for years, even in the event the '405 patent is invalidated at the Federal Circuit.

To prevent such an inequitable outcome, HEC respectfully requests that this Court exercise its discretion to stay the effect of the statute, thus preventing the reset of the FDA's approval of HEC's ANDA and maintaining the current *status quo*. If HEC's appeal is successful (which HEC expects will be the case), then HEC would not suffer irreparable harm posed by the delay in market entry while awaiting the FDA's conversion of tentative approval to final approval

[1] https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=A&Appl_No=207939#37196

(again). In fact, the Federal Circuit has already previewed its position on the same issue and same patent presented here. Based on oral argument from early 2020 in an IPR on the very same patent, a Federal Circuit panel expressed skepticism of certain of Novartis' positions asserted in this litigation and upheld by this Court. HEC's appeal will be the second time for the Federal Circuit to consider certain validity issues and specifically the lack of disclosure of the negative claim limitation "absent the immediately preceding loading dose" in the specification – and this time the Federal Circuit should have the opportunity to render an opinion on the merits following oral argument. Dkt. 696, Ex. 6; Dkt. 743 at 4. For this and other reasons, HEC is likely to succeed on the merits. Importantly, Novartis will not be at all prejudiced or tactically disadvantaged by a stay – Novartis is and will remain the sole purveyor of fingolimod on the U.S. market and HEC remains permanently enjoined. Dkt. 780 (¶4). Indeed, a stay of the section 271(e)(4)(A) portion of the order is the only way to preserve the *status quo* of both parties pending appeal and ***not*** unduly prejudice HEC.

## ARGUMENT

### I. THIS COURT SHOULD EXERCISE ITS DISCRETION AND STAY THE RESET OF THE EFFECTIVE DATE OF HEC'S FINAL APPROVAL OF ITS ANDA PENDING HEC'S APPEAL TO THE FEDERAL CIRCUIT

Pursuant to 35 U.S.C. § 271(e)(4)(A), the effective date of any final approval by the FDA of HEC's ANDA No. 207939 shall be a date not earlier than the expiration date of the '405 patent. Dkt. 780 (¶4). The '405 patent does not expire until 2027. HEC received the FDA's first generic approval for a generic fingolimod product in December 2019 [https://www.fda.gov/news-events/press-announcements/fda-approves-first-generics-gilenya]. An order delaying the effective date of FDA approval is, as Judge Posner has explained, "a form

of patent injunction." *See SmithKline Beecham Corp. v. Apotex Corp*., 247 F. Supp. 2d 1011, 1050 (N.D. Ill. 2003), *aff'd on other grounds*, 403 F.3d 1331 (Fed. Cir. 2005).

This Court should exercise its discretion and grant HEC's request for a stay as to the reset of the effective date of HEC's final approval pending appeal to the Federal Circuit based on the following factors: (1) HEC is likely to succeed on the merits; (2) HEC will be irreparably injured absent a stay; (3) Novartis will not be substantially injured or disadvantaged by such a stay; and (4) the public interest supports a stay. *See Standard Havens Prods., Inc. v. Gencor Indus., Inc.*, 897 F.2d 511, 512 (Fed. Cir. 1990), *cert denied*, 506 U.S. 817 (1992) (citing *Hilton v. Braunskill*, 481 U.S. 770, 776 (1987)). Each factor need not be given equal weight and the strength of one factor may diminish the showing necessary for another. *See Standard Havens*, 897 F.2d at 512-13. All of the factors support a stay, preventing section 271(e)(4)(A) from becoming effective, and allowing HEC to maintain its final FDA approval pending appeal.

**A. HEC Is Likely To Succeed On The Merits**

In its focused appeal, HEC will contend that that the '405 patent is invalid. In order to meet the requirements for the requested partial stay, HEC need only show "a reasonable chance, or probability, of winning" although such showing need not be "more likely than not." *Singer Mgmt. Consultants, Inc. v. Milgram*, 650 F.3d 223, 229 (3d Cir. 2011) (*en banc*); *see also In re Revel AC, Inc.*, 802 F.3d 558, 571 (3d Cir. 2015) (collecting cases) (significantly better than negligible but not greater than 50%). HEC has not only a reasonable chance of showing the '405 patent is invalid on appeal for lack of written description but it is likely to succeed on the merits[2]:

[2] HEC reserves all rights with respect to its appeal and the basis/evidence covered in this abbreviated motion should not be viewed as limiting by Novartis.

1. Lack of written description for the negative claim limitation.

It is undisputed that every claim of the '405 patent contains the same language for its negative limitation: 0.5 mg fingolimod administered "absent an immediately preceding loading dose regimen." Dkt. 743 at 4.[3] It is well settled that for a negative claim limitation to satisfy the written description requirement, the specification must describe "a reason to exclude the relevant limitation." *Santarus, Inc. v. Par Pharm, Inc.*, 694 F.3d 1344, 1351 (Fed. Cir. 2012). The "reason to exclude" standard may be met where disadvantages of using the excluded limitation are described or via a description of alternative features. *See Inphi Corp. v. Netlist, Inc.*, 805 F.3d 1350, 1356 (Fed. Cir. 2015). Here, the '405 patent specification does not satisfy the bare requirements for written description on a negative claim limitation, as articulated by the Federal Circuit.

The '405 patent fails to describe or identify a single reason to exclude an immediately preceding loading dose. Dkt. 743 at 5. This is no surprise as the language "absent an immediately preceding loading dose regimen" was belatedly added to the claims many years after the original disclosure was filed. Dkt. 743 at 8. This Court agreed with this factual premise in its findings of fact, recognizing that the patent plainly "***does not describe loading doses***." Dkt. 769 at ¶ 65, p. 22 (emphasis added). Yet this Court contradicted its own factual findings when it also concluded that "the Patent ***describes*** a daily dosage of 0.5 mg of fingolimod, ***without a preceding loading dose***, to treat RRMS." Dkt. 769 at ¶ 24, p. 32 (emphasis added). In so finding, Federal Circuit precedent that the negative claim limitation be disclosed went wholly ignored. Ignoring the proper legal principles - which themselves do not

[3] To the extent HEC cites to documents already on file with this Court, including, for example, post-trial briefing, HEC incorporates by reference the underlying evidence in the record cited to in such briefing and in the record before this Court.

support this Court's conclusions as the '405 patent disclosure - is a basis for reversal. *Spectrum Pharm., Inc. v. Sandoz Inc.*, 802 F.3d 1326, 1333 (Fed. Cir. 2015) (a factual finding is clearly erroneous if, upon review of the evidence, a reviewing court is "left with the definite and firm conviction that a mistake has been made."); *Inwood Labs, Inc. v. Ives Labs, Inc.*, 456 U.S. 844, 855 (1982) ("[I]f the trial court bases its findings upon a mistaken impression of applicable legal principles, the reviewing court is not bound by the clearly erroneous standard.").

Furthermore, this Court appeared to rely on the knowledge of a person of ordinary skill in the art ("POSA") to supplant the patent disclosure, finding that the absence of an immediately preceding loading dose from the specification and the Prophetic Trial would tell a POSA that "loading doses are excluded from the invention." Dkt. 769, ¶ 61 at p. 21. Based this knowledge imputed to a POSA, this Court found that the '405 patent "provides a sufficient written description of the invention such that a person of ordinary skill would know that the inventors were in possession of the invention." Dkt. No. 769, ¶ 24 at p. 32. Yet, Novartis' own witnesses, testifying as POSAs, contradicted this finding. Dkt. No. 743 at 9. For example, Novartis' expert Dr. Lublin, an MS physician involved in the human clinical trials for fingolimod, testified that the 0.5 mg dosage does not necessarily exclude a loading dose from the perspective of a POSA (Dkt. No. 743 at 9 (citing Lublin 294:25-295:4)). Indeed, Novartis' expert in pharmacology, Dr. Jusko, who conducted fingolimod studies to develop animal models even testified that he plainly could "envision the possibility of starting with a loading dose" (Dkt. No. 743 at 9 (citing Jusko 896:18-25)) and several experts testified that it was not unheard of to use a loading dose in the treatment of multiple sclerosis. Dr. Lublin testified that drugs with a long half-life, such as fingolimod, would be candidates for loading doses, that fingolimod loading doses have been used in transplant patients, and that a POSA would use a loading dose to treat chronic immune

disorders like MS. Dkt. No. 743 at 12 (citing Lublin 201:22-202:2; 202:14-21); Dkt. 744 at p. 12-13. Dr. Jusko walked back previous testimony that a POSA would not have considered using a loading dose when looking to design a fingolimod dosing regimen for MS. Dkt. 743 at 13; Dkt. 744 at 12 (citing Jusko 897:14-898:4; 932:15-933:6). HEC's expert, Dr. Hoffman, a treating physician, testified consistent with Novartis' experts, that a loading dose might be used for chronic MS and the long half-life of fingolimod makes it a candidate for use of a loading dose. Dkt. 743 at 13; Dkt. 744 at 14. Regardless of these contradictions, the Federal Circuit has made clear that written description is an "objective inquiry into the four corners of the specification," and "it is the ***specification itself*** that must ***demonstrate possession*** [by disclosure]" of the invention. *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351-1352 (Fed. Cir. 2010) (*en banc*) (emphasis added); *see also Alcon Research Ltd. v. Barr Labs., Inc.*, 745 F.3d 1180, 1190 (Fed. Cir. 2019) (whether claim satisfies written description is clear error). Here, the specification does not rise to the occasion.

HEC's strong likelihood of prevailing on the lack of written description is not only based on the record in this case, but the ***Federal Circuit has already been presented with this issue*** as it relates to a decision issued by the PTAB on an IPR petition relating to this '405 patent and, based on oral argument in that matter, ***the Panel expressed strong skepticism*** that there is any support for the negative limitation in the specification. Dkt. 743 at 4; Dkt. 696, Ex. 6. This is apparent from the following excerpts from the transcript:

> MS. LOVE [Novartis' Counsel]: … The test for sufficient written description is whether the disclosure of an application reasonably conveys to those skilled in the art that the inventor had possession of the invention as of the filing date.

> THE COURT: But this is a claim limitation and it isn't found in [the] 2006 application.
>
> MS. LOVE: Well, Your Honor –
>
> THE COURT: --it's not a question of heightened or lowered. ***It's just not there.***

Dkt. 696, Ex. 6 at 12:18-13:6 (emphasis added); *see also id.* at 13:19-21 ("THE COURT: But wouldn't you say that even the negative limitation has to find support in the specification?"); *see id.* at 17:2-11 ("THE COURT: --so—so is it your argument that the reason to exclude can be inherent in the specification? . . . doesn't – doesn't that leave a person of skill in the art guessing an – and just searching for the needle in the hay stack?"). Novartis, undoubtedly seeing the writing on the wall, settled with the remaining appellants who still held standing shortly after the oral argument. Novartis was able to moot the written description issue prior to any written opinion by focusing the Federal Circuit to the threshold standing issue as to the only remaining the appellant. Dkt. 749. Nevertheless, a Federal Circuit panel has been presented with this written description issue and, based on oral argument and the plain disclosure of the patent on its face, it appears the Federal Circuit favors HEC's position over Novartis', further bolstering HEC's position that it is likely to succeed on the merits. Dkt. 743 at 4.

2. Lack of written description for the 0.5 mg daily dosage in humans.

Additionally, the '405 patent fails to provide adequate written description support for the 0.5 mg daily dose required by the claims. Dkt. 743 at p. 14. Just as support for written description comes from the four corners of the specification, so too does possession of the invention. *Centocor Ortho Biotech, Inc. v. Abbott Labs.*, 636 F.3d 1341, 1348 (Fed. Cir. 2011) (citations omitted). Possession of the invention at the time of filing is demonstrated by the disclosure in the specification. *See Idenix Pharmas. LLC v. Gilead Sciences, Inc.*, 941 F.3d 1149, 1163 (Fed.

Cir. 2019). Actual or constructive possession, without proper disclosure, does not meet the written description requirement, particularly in the pharmaceutical industry. *See Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 969 (Fed. Cir. 2002); *Ariad*, 598 F.3d at 1353. The '405 patent describes some results of an Experimental Autoimmune Encephalomyelitis ("EAE") experiment in animals, but there is no disclosure supporting the claimed 0.5 mg human dosage. Dkt. 743 at 21. This Court found that the EAE experiment disclosed in the specification (which experiment induced a disease that merely "***mimics***" relapsing remitting multiple sclerosis ("RRMS") in ***Lewis rats, not humans***) provided on its face that 0.3 mg/kg of fingolimod be given once a week, but there is no factual finding that the disclosure expressly provided for the administration of 0.5 mg daily to humans with RRMS. Dkt. 769 at ¶ 5, p. 5 (emphasis added). This Court also found that the Prophetic Trial disclosed in the specification (but not actually conducted) described an example where RRMS patients receive fingolimod at a daily dosage of 0.5 mg for two to six months. Dkt. 769 at ¶ 4, p. 4-5; ¶ 51 (the Prophetic Trial disclosed in the specification was not actually conducted). Thus, based on a combination of the EAE animal experiment in the specification cobbled together with six sentences of a Prophetic Trial (from which this Court found that a POSA would only at best "***assume*** that the daily dosage of 0.5 mg is an effective treatment") (Dkt. 769, ¶ 49, p. 16) (emphasis added), this Court concluded that the '405 patent provides a "sufficient written description of the invention such that the person of ordinary skill in the art would know that the inventors were in possession of the invention." Dkt. 769, ¶ 24, p. 32. But the Prophetic Trial was never conducted and a "desired outcome" is not sufficient to satisfy written description requirements under the law, particularly where, as here, there is no descriptive link to the invention. *See CreAgri, Inc. v. Pinnaclelife, Inc.*, 2013 WL 6673676, at *12-13 (N.D. Cal. Dec. 18, 2013), *aff'd*, 579 F. App'x 1003 (Fed. Cir. 2014).

**B. If The Reset Is Not Stayed, Then HEC Will Be Irreparably Harmed**

If this Court does not stay the reset of the approval of HEC's ANDA, then HEC will be irreparably harmed. *See Winter v. Natural Res. Def. Council, Inc.*, 555 U.S. 7, 22 (2008); *see also In re Revel AC*, 802 F.3d at 569. Without a stay, even if the Federal Circuit invalidates the '405 patent, HEC would not be in a position to timely enter the market because its final FDA approval would be delayed and HEC would need to once again seek final approval from the FDA. Such an endeavor on the second go-around would be a needless allocation of both HEC and the FDA's time and resources. Furthermore, with the delay imposed by any reset of the final approval, HEC would lose any benefit of quick entry to the market in the event the '405 patent is invalidated – and quick entry of a generic upon invalidation of patents is a well-known core tenet of Hatch-Waxman litigations. Accordingly, without a stay HEC would be irreparably harmed and would have no recourse to recoup its substantial loss. Conversely, a stay would allow HEC to preserve its ability to timely enter the market should the '405 patent be invalidated by the Federal Circuit in due course.

**C. Novartis Will Neither Be Unduly Prejudiced Nor Tactically Disadvantaged By A Stay**

In contrast, the stay of the reset of final approval of HEC's ANDA under section 271(e)(4)(A) does not prejudice Novartis and would not tactically disadvantage Novartis. Novartis remains the sole purveyor of fingolimod in the U.S. market and enjoys all the benefits of the permanent injunction against HEC. In fact, unless and until the '405 patent is invalidated at the Federal Circuit, Novartis remains in ***exactly the same position whether or not this stay is granted.***

**D. Public Interest Weighs In Favor Of A Stay**

The public interest is best served through making generic fingolimod available as soon as the legal barriers on Novartis' patent have been resolved. Accordingly, the public interest lies in maintaining *status quo* pending appeal, thus allowing HEC to take advantage of the FDA's final approval of its generic fingolimod product immediately following HEC's success on appeal or the expiration of the '405 patent, whichever occurs first.

## CONCLUSION

Based on the foregoing, HEC respectfully asks that this Court partially stay execution of the Final Judgment with respect to the reset of approval of HEC's ANDA under 35 U.S.C. § 271(e)(4)(A); such a stay is in this Court's discretion and would preserve status quo pending appeal.

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Dated: September 25, 2020

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**CERTIFICATE OF SERVICE**

I hereby certify that on September 25, 2020, I caused the foregoing to be electronically filed with the Clerk of the Court using CM/ECF, which will send notification of such filing to all registered participants.

/s/ *Stamatios Stamoulis*
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